REMARKS

Claims 1, 3-4, 6-8, 10, 12-13 and 19 are pending in the instant application. Claims 1, 3-4, 6-8, 10, 12-13 and 19 have been rejected by the Examiner. By the above amendment, Claim 10 has been amended to more particularly point out and distinctly claim the subject matter which applicants regard as the invention. More particularly, independent Claim 10 has been amended to limit the indication to Alzheimer's dementia. Applicants submit that the amendments to the claims are supported by the specification as filed, for example, at page 4, lines 36-37. After entry of the amendments, Claim 1, 3-4, 6-8, 10, 12-13 and 19 will remain pending and under consideration.

The Examiner has rejected Claims 1, 3-4, 6-8, 10, 12-13 and 19 under 35 U.S.C. §103(a) as being unpatentable over Wilkinson et al. in view of Yankner et al. (US Patent No. 6,080,778) and WO95/06470. The Examiner alleges that the cited prior art references disclose the treatment of Alzheimer's disease (hereinafter "AD") with 24 mg/day of galantamine and the use of statins for the treatment of AD, and that one of ordinary skill in the art would have been motivated to combine the prior art with the expectation that the combination would be effective for treatment of AD. The Examiner points out that Claims 10, 12, 13 and 19 are not limited to AD but encompass any type of dementia. With regard to the Declaration of Dr. Joan Amatniek, the Examiner asserts there is insufficient evidence to establish a synergistic effect with respect to the combination of galantamine and statin since the original trials were not designed to ensure sufficient statistical power to assess the effect of statins, the administration of statins was heterogenous with respect to specific statin, dose and treatment duration and the follow up was limited to 5 to 6 months which may be insufficient for comparing effects of statins and galantamine. The Examiner concludes:

> As such, it cannot be concluded from the data that the combination of galantamine and statin is synergistic much less synergistic over the entire scope of the claims which encompasses any statin and/or dose of statin.
>
> Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Applicants respectfully traverse this rejection. By the above amendments, independent Claim 10 has been amended to limit the dementia to Alzheimer's dementia. By effect of their dependence from Claim 10, dependent Claims 12, 13 and 19 also possess this limitation. Applicants urge that the claimed invention possesses unexpected advantages which were not suggested by the prior art and which could not have been predicted by one of ordinary skill in the art. As Dr. Amatniek's declaration shows, on the basis of post hoc analyses of several double blind clinical trials of galantamine hydrobromide, Applicants surprisingly found that there was a synergistic positive effect on cognitive function in patients receiving galantamine + statin, as compared to those receiving either galantamine alone or placebo + statin. *See*, Amatniek Decl. ¶¶ 8, 10, 12, 14. Additionally, the data from the initial pivotal trials (GAL-INT1, GAL-USA-1 and GAL-USA-10) unexpectedly and surprisingly showed that patients receiving galantamine + statin were above their baseline scores for 4 more months compared to patients receiving galantamine alone, which is also consistent with a synergistic effect; patients receiving galantamine + statin returned to their original cognitive status at approximately 14 months, as compared to 10 months for the patients on galantamine alone and 3 months for patients on placebo + statin. *See*, Amatniek Decl. ¶¶ 8, 10, 14. Furthermore, at 18 and 24 months, a sustained efficacy difference in favor of galantamine + statin compared to galantamine alone appears to exist, which is also consistent with a synergistic effect. *See*, Amatniek Decl. ¶¶ 8, 10, 14. These unexpected findings rebut any *prima facie* case of obviousness, as one of ordinary skill in the art at the time the invention was made would not have expected the combination of galantamine + statin to have a synergistic effect on cognitive function of AD patients, or to delay by an additional 4 months the time to cross baseline as compared to patients receiving galantamine alone.

Even *assuming arguendo* that the data fail to show a synergistic effect, Applicants submit that these results (as discussed above and set forth in detail in Dr. Amatniek's Declaration) are greater than those which would have been expected from the cited prior art to an unobvious extent, and that the results are of a significant, practical advantage. In fact, when the data from the post hoc analyses were presented to nine experts in the field of statins, galantamine, and Alzheimer's disease during the first two weeks of June 2007 under terms of confidentiality, the experts were, in fact, surprised by the findings. *See*, Amatniek Decl. ¶¶ 14. As such, Applicants maintain that the claimed invention as a whole would not have been obvious to one of ordinary

skill in the art at the time the invention was made and Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-14 and 19 under 35 U.S.C. §103(a).

In view of the above amendments and remarks, Applicants maintain that the application is in condition for allowance and passage to issue is earnestly requested.

Respectfully submitted,

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Dated: October 28, 2008